Department of Veterans Affairs

Agent Orange Brief

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AGENT ORANGE AND SOFT TISSUE SARCOMAS

What are soft tissue sarcomas?

Soft tissue sarcomas are a group of different types of malignant tumors which arise from body tissues such as muscle, fat, blood and lymph vessels and connective tissues (that is, distinct from hard tissue such as bone or cartilage). These tumors are relatively rare.

In regulations, VA has defined the term "soft tissue sarcoma" to include adult fibrosarcoma; dermatofibrosarcoma protuberans, malignant fibrous histiocytoma, liposarcoma; leiomyosarcoma; epithelioid leiomyosarcoma (malignant leiomyoblastoma); rhabdomyosarcoma; ectomesenchymoma; angiosarcoma (hemangiosarcoma and lymphangiosarcoma); proliferating (systemic) angioendotheliomatosis; malignant glomus tumor; malignant hemangiopericytoma; synovial sarcoma (malignant synovioma); malignant giant cell tumor of tendon sheath; malignant schwannoma, including malignant schwannoma with rhabdomyoblastic differentiation (malignant Triton tumor), glandular and epithelioid malignant schwannomas; malignant mesenchymoma; malignant granular cell tumor; alveolar soft part sarcoma; epithelioid sarcoma; and clear cell sarcoma of tendons and aponeuroses. (See 56 Fed. Reg. 51651, October 15, 1991).

Why are Vietnam veterans concerned about soft tissue sarcomas?

The possibility that exposure to phenoxy herbicides, such as Agent Orange, may have caused rare forms of cancer in humans such as soft tissue sarcomas was suggested in 1979 and 1981 by small scale studies conducted in Sweden. These studies showed that persons reporting occupational exposure to phenoxy herbicides may have a 5 to 6 fold higher risk of developing soft tissue sarcomas as compared to persons without such exposure.

Have more recent research results supported or conflicted with the Swedish studies finding regarding soft tissue sarcomas?

A number of scientific studies of soft tissue sarcomas among people who may have been exposed to herbicides and/or dioxins have been published in the past few years. Some studies suggested a possible association between

these exposures and an increased risk of some cancers, but none showed an increased risk of soft tissue sarcomas of the magnitude cited by the Swedish researchers, and the majority of these investigations showed no association at all.

Mortality studies conducted by Massachusetts and West Virginia indicated that there might be a link between service in Vietnam and soft tissue sarcomas. However, the small number of deaths in the West Virginia study makes it possible that these findings were the results of chance rather than real association.

A New York State study showed that fewer Vietnam veterans died of soft tissue sarcomas than Vietnam-era veterans who did not serve in Vietnam. A study in New Zealand of soft tissue sarcomas and exposure to phenoxy herbicides and chlorophenols, a National Cancer Institute study of agricultural herbicide use and risk of lymphomas and soft tissue sarcomas in Kansas, a western Washington State study, the Department of Veterans Affairs (VA) Vietnam veterans mortality study, two VA studies of the relationship between soft tissue sarcomas and military service in Vietnam, and the Centers for Disease Control Selected Cancers Study have not supported the findings of the Swedish researchers. The VA studies were published in the Journal of Occupational Medicine in December 1986, and the Journal of the National Cancer Institute in October 1987. Very few cases of soft tissue sarcomas are appearing in the Agent Orange Registry. Research on soft tissue sarcomas and other cancers is continuing.

What did the Veterans' Advisory Committee on Environmental Hazards conclude about the relationship between herbicides and soft tissue sarcomas?

This VA committee, established by law, met on May 16-17, 1990, to review scientific literature relating to whether there is a significant statistical association between exposure to a dioxin-containing herbicide and subsequent development of soft tissue sarcomas. After considering more than eighty articles, the Advisory Committee concluded that it was as least as likely as not that such an association existed.

Committee members noted that work done in Sweden was strongly compelling for an association while studies done elsewhere not showing an association were also very strong. Members observed that "positive" studies tended to be confined to one geographic area of the world whereas studies involving Vietnam veterans did not find such an association. Several Committee members noted they did not believe that the scientific evidence demonstrated a causal association.

How did VA respond to the Advisory Committee's finding?

The day after the meeting, Secretary Derwinski announced that VA would recognize, as service-connected, soft tissue sarcomas based on exposure to dioxin-containing herbicides.

Final rule implementing the Secretary's decision was published in the Federal Register in October 1991. (See 56 Fed. Reg. 51651, October 15, 1991).

How did Public Law 102-4 help Vietnam veterans who suffer with soft tissue sarcomas?

To a large extent, Public Law 102-4, the Agent Orange Act of 1991, enacted February 6, 1991, codified (established in law) the Secretary's decision. However, since there are significant differences in the eligibility requirements for service connection under the rule and the presumptions of service connection established under Public Law 102-4, the rule implementing the new statute was published separately in the Federal Register. (For proposed rule, see 57 Fed. Reg. 30707, July 10, 1992; for final rule see 58 Fed. Reg. 29107, May 19, 1993).

What did the National Academy of Sciences (NAS) conclude about soft tissue sarcomas (STS) in its 1993 report, entitled Veterans and Agent Orange - Health Effects of Herbicides Used in Vietnam?

The 832-page NAS report contained the following statements:

> The strongest evidence for an association between STS and exposure to phenoxy herbicides come from a series of case-control studies involving a total of 506 cases conducted by Hardell and colleagues in Sweden ... that show an association between STS and exposure to phenoxy herbicides, chloropenols, or both. Although these studies have been criticized, the committee feels that there is insufficient justification to discount the consistent pattern of elevated risks, and the clearly described and sound methods employed.
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> These findings are supported by a significantly increased risk in the NIOSH study ... for the production workers most highly exposed to TCDD ... , and a similar increased risk in the IARC cohort ... for deaths that occurred between 10 and 19 years after the first exposure .... These are the two largest, as well as the most highly exposed occupational cohorts.
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> Some studies in other occupational, environmental, and veterans group showed an increased risk for STS, but the results were commonly nonsignificant possibly because of small sample sizes related to the relative rarity of STS in the population, except for males in Zone R of Seveso. The risk of this group was significantly elevated and is consistent with the findings supporting an association....
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> Evidence is sufficient to conclude that there is a positive association between exposure to herbicides (2,4-D; 2,4,5-T and its contaminant TCDD; cacodylic acid; and picloram) and soft tissue sarcoma.

What did the NAS conclude regarding soft tissue sarcomas in its 1996 update?

In the 1996 update, the NAS commented that reports issued since the publication of **Veterans and Agent Orange** provide “additional evidence for an association” between exposure to herbicides and soft tissue sarcomas.

What did the NAS conclude regarding soft tissue sarcomas in its 1998 update?

The 1998 update contained the following statement, “No new evidence has been produced to change the committee’s earlier judgment that evidence is sufficient to conclude that a positive statistical association exists between exposure” to the herbicides considered in this report and soft tissue sarcomas.

Where can a veteran get additional information on this subject?

Information on soft tissue sarcomas and related matters can be obtained at VA medical center libraries, from the Registry Physicians at every VA medical center, or from the Environmental Agents Service (131), Department of Veterans Affairs, 810 Vermont Avenue, N.W., Washington, DC 20420.